DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring, MD 20993

April 22, 2013

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Director
Centers for Disease Control and Prevention
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Dear Dr. Frieden:

This letter is in response to your request that the Food and Drug Administration (FDA) issue an Emergency Use Authorization (EUA) for emergency use of the CDC Human Influenza Virus Real-Time RT-PCR Diagnostic Panel-Influenza A/H7 (Eurasian Lineage) Assay for the presumptive detection of novel influenza A(H7N9) virus in conjunction with the FDA cleared CDC Human Influenza Virus Real-Time RT-PCR Diagnostic Panel in real-time RT-PCR (rRT-PCR) assays in patients with signs and symptoms of respiratory infection, pursuant to section 564 of the Federal Food, Drug, and Cosmetic Act (the Act) (21 U.S.C. § 360bbb-3), by public health and other qualified laboratories.

On April 19, 2013, pursuant to section 564(b)(1)(C) of the Act (21 U.S.C. § 360bbb-3(b)(1)(C)), the Secretary of the Department of Health and Human Services (HHS) determined that there is a significant potential for a public health emergency that has a significant potential to affect national security or the health and security of United States citizens living abroad, and that involves a biological, chemical, radiological, or nuclear agent or agents, or a disease or condition that may be attributable to such an agent or agents - in this case, novel influenza A(H7N9) virus.[1] Pursuant to section 564(b)(1) of the Act (21 U.S.C. § 360bbb-3(b)(1)), and on the basis of such determination, the Secretary of HHS then declared that circumstances exist justifying the authorization of the emergency use of *in vitro* diagnostics for the detection of A(H7N9) influenza virus, subject to the terms of any authorization issued under 21 U.S.C. § 360bbb-3(a). [2]

Having concluded that the criteria for issuance of this authorization under section 564(c) of the Act (21 U.S.C. § 360bbb-3(c)) are met, I am authorizing the emergency use of the CDC Human Influenza Virus Real-Time RT-PCR Diagnostic Panel-Influenza A/H7 (Eurasian Lineage) Assay (as described in the scope section of this letter (Section II)) for the presumptive detection of A(H7N9) influenza virus in patients with signs and symptoms of respiratory infection, subject to the terms of this authorization.

I. Criteria for Issuance of Authorization

[1] As amended by the Pandemic and All-Hazards Preparedness Reauthorization Act, Pub. L. No. 113-5, under section 564(b)(1)(C) of the Act the Secretary may make a determination of a public health emergency, or of a significant potential for a public health emergency.

[2] Memorandum, Determination of a Significant Potential for a Public Health Emergency and Declaration that Circumstances Exist Justifying an Authorization Pursuant to Section 564 of the Federal Food, Drug, and Cosmetic Act (April 19, 2013).

I have concluded that the emergency use of the CDC Human Influenza Virus Real-Time RT-PCR Diagnostic Panel-Influenza A/H7 (Eurasian Lineage) Assay for the presumptive detection of A(H7N9) influenza virus in patients with signs and symptoms of respiratory infection meets the criteria for issuance of an authorization under section 564(c) of the Act, because I have concluded that:

1. The A(H7N9) influenza virus can cause influenza, a serious or life threatening disease or condition to humans infected by this virus;

2. Based on the totality of scientific evidence available to FDA, it is reasonable to believe that the CDC Human Influenza Virus Real-Time RT-PCR Diagnostic Panel-Influenza A/H7 (Eurasian Lineage) Assay may be effective in diagnosing A(H7N9) influenza virus, and that the known and potential benefits of the CDC Human Influenza Virus Real-Time RT-PCR Diagnostic Panel-Influenza A/H7 (Eurasian Lineage) Assay, when used for diagnosing A(H7N9) influenza virus infection, outweigh the known and potential risks of such product; and

3. There is no adequate, approved, and available alternative to the emergency use of the CDC Human Influenza Virus Real-Time RT-PCR Diagnostic Panel-Influenza A/H7 (Eurasian Lineage) Assay for diagnosing A(H7N9) influenza virus.[3]

II. Scope of Authorization

I have concluded, pursuant to section 564(d)(1) of the Act, that the scope of this authorization is limited to the use of the authorized CDC Human Influenza Virus Real-Time RT-PCR Diagnostic Panel-Influenza A/H7 (Eurasian Lineage) Assay for the presumptive detection of A(H7N9) influenza virus in patients with signs and symptoms of respiratory infection.

The Authorized CDC Human Influenza Virus Real-Time RT-PCR Diagnostic Panel-Influenza A/H7 (Eurasian Lineage) Assay:

The CDC Human Influenza Virus Real-Time RT-PCR Diagnostic Panel-Influenza A/H7 (Eurasian Lineage) Assay is a real-time reverse transcriptase PCR (rRT-PCR) for the *in vitro* qualitative detection and differentiation of A(H7N9) influenza viral RNA in upper respiratory tract specimens, such as nasopharyngeal swabs (NPS), nasal swabs (NS), throat swabs (TS), nasal aspirates (NA), nasal washes (NW), and dual nasopharyngeal/throat swabs (NPS/TS) and lower respiratory tract specimens (including bronchoalveolar lavage (BAL), bronchial wash (BW), tracheal aspirate (TA), sputum, and lung tissue from patients with signs and symptoms of respiratory infection. The testing procedure consists of nucleic acid extraction followed by rRT-PCR on the FDA cleared Applied Biosystems 7500 Fast Dx Real-Time PCR Instrument.

The CDC Human Influenza Virus Real-Time RT-PCR Diagnostic Panel-Influenza A/H7 (Eurasian Lineage) Assay includes the following primer and probe sets:

- **INF A:** Primers and probe target the gene encoding the Matrix protein to detect all influenza A strains, but do not detect influenza B strains
- **EuH7**: Primers and probe target the gene encoding the HA protein to detect influenza A/H7 (Eurasian Lineage) virus strains

[3] No other criteria of issuance have been prescribed by regulation under section 564(c)(4) of the Act.

- **Extraction/Process Control: RP**: Primers and probe detect the human RNase P gene sequence and are used with human clinical specimens to indicate that adequate isolation of nucleic acid resulted from the extraction of the clinical specimen.

The CDC Human Influenza Virus Real-Time RT-PCR Diagnostic Panel-Influenza A/H7 (Eurasian Lineage) Assay also includes the following control materials:

- **No Template Control (NTC)**
- **Human Specimen Control (HSC)**
- **Influenza A/H7 (Eurasian Lineage) Positive Control (EuH7PC)**

The above described CDC Human Influenza Virus Real-Time RT-PCR Diagnostic Panel-Influenza A/H7 (Eurasian Lineage) Assay, when labeled consistently with the labeling authorized by FDA, entitled "CDC Human Influenza Virus Real-Time RT-PCR Diagnostic Panel-Influenza A/H7 (Eurasian Lineage) Assay Instructions for Use" (available at http://www.fda.gov/MedicalDevices/ Safety/EmergencySituations/ucm161496.htm), which may be revised with written permission of FDA, is authorized to be distributed to and used by public health and other qualified laboratories under this EUA, despite the fact that it does not meet certain requirements otherwise required by federal law.

The above described CDC Human Influenza Virus Real-Time RT-PCR Diagnostic Panel-Influenza A/H7 (Eurasian Lineage) Assay is authorized to be accompanied by the following information pertaining to the emergency use, which is authorized to be made available to healthcare providers and patients:

- **Fact Sheet for Healthcare Providers: Interpreting CDC Human Influenza Virus Real-Time RT-PCR Diagnostic Panel-Influenza A/H7 (Eurasian Lineage) Assay Test Results**

- **Fact Sheet for Patients: Understanding Results from CDC Human Influenza Virus Real-Time RT-PCR Diagnostic Panel-Influenza A/H7 (Eurasian Lineage) Assay**

As described in section IV below, CDC is also authorized to make available additional information relating to the emergency use of the authorized CDC Human Influenza Virus Real-Time RT-PCR Diagnostic Panel-Influenza A/H7 (Eurasian Lineage) Assay that is consistent with, and does not exceed, the terms of this letter of authorization.

I have concluded, pursuant to section 564(d)(2) of the Act, that it is reasonable to believe that the known and potential benefits of the authorized CDC Human Influenza Virus Real-Time RT-PCR Diagnostic Panel-Influenza A/H7 (Eurasian Lineage) Assay in the specified population, when used for presumptive detection of A(H7N9) influenza virus, outweigh the known and potential risks of such a product.

I have concluded, pursuant to section 564(d)(3) of the Act, based on the totality of scientific evidence available to FDA, that it is reasonable to believe that the authorized CDC Human Influenza Virus Real-Time RT-PCR Diagnostic Panel-Influenza A/H7 (Eurasian Lineage) Assay may be effective in the diagnosis of A(H7N9) influenza virus infection pursuant to section 564(c)(2)(A) of the Act. The FDA has reviewed the scientific information available including the information supporting the conclusions described in Section I above, and concludes that the authorized CDC Human Influenza Virus Real-Time RT-PCR Diagnostic Panel-Influenza A/H7

(Eurasian Lineage) Assay, when used to diagnose A(H7N9) influenza virus infection in the specified population, meets the criteria set forth in section 564(c) of the Act concerning safety and potential effectiveness.

The emergency use of the authorized CDC Human Influenza Virus Real-Time RT-PCR Diagnostic Panel-Influenza A/H7 (Eurasian Lineage) Assay under this EUA must be consistent with, and may not exceed, the terms of this letter, including the scope and the conditions of authorization set forth below. Subject to the terms of this EUA and under the circumstances set forth in the Secretary of HHS's determination under section 564(b)(1)(C) described above and the Secretary of HHS's corresponding declaration under section 564(b)(1), the CDC Human Influenza Virus Real-Time RT-PCR Diagnostic Panel-Influenza A/H7 (Eurasian Lineage) Assay described above is authorized to diagnose A(H7N9) influenza virus infection in patients with signs and symptoms of respiratory infection.

This EUA will cease to be effective when the declaration of emergency is terminated under section 564(b)(2) of the Act or when the EUA is revoked under section 564(g) of the Act.

III. Waiver of Certain Requirements

I am waiving the following requirements for the CDC Human Influenza Virus Real-Time RT-PCR Diagnostic Panel-Influenza A/H7 (Eurasian Lineage) Assay during the duration of this emergency use authorization:

- Current good manufacturing practice requirements, including the quality system requirements under 21 CFR Part 820 with respect to the design, manufacture, packaging, labeling, storage, and distribution of the CDC Human Influenza Virus Real-Time RT-PCR Diagnostic Panel-Influenza A/H7 (Eurasian Lineage) Assay.

- Labeling requirements for cleared, approved, or investigational devices, including labeling requirements under 21 CFR 809.10 and 809.30, except for the intended use statement (21 CFR 809.10(a)(2), (b)(2)), adequate directions for use (21 U.S.C. 352(f)), (21 CFR 809.10(b)(5) and (8)), any appropriate limitations on the use of the device including information required under 21 CFR 809.10(a)(4), and any available information regarding performance of the device, including requirements under 21 CFR 809.10(b)(12).

IV. Conditions of Authorization

Pursuant to section 564 of the Act, I am establishing the following conditions on this authorization:

CDC

A. CDC will distribute the authorized CDC Human Influenza Virus Real-Time RT-PCR Diagnostic Panel-Influenza A/H7 (Eurasian Lineage) Assay with the authorized labeling, as may be revised with written permission of FDA, only to public health and other qualified laboratories.

B. CDC will provide to the public health and other qualified laboratories the authorized CDC Human Influenza Virus Real-Time RT-PCR Diagnostic Panel-Influenza A/H7 (Eurasian Lineage) Assay Fact Sheet for Healthcare Providers and the authorized CDC Human Influenza Virus Real-Time RT-PCR Diagnostic Panel-Influenza A/H7 (Eurasian Lineage) Assay Fact Sheet for Patients.

C. CDC will make available on its website the authorized CDC Human Influenza Virus Real-Time RT-PCR Diagnostic Panel-Influenza A/H7 (Eurasian Lineage) Assay Fact Sheet for Healthcare Providers and the authorized CDC Human Influenza Virus Real-Time RT-PCR Diagnostic Panel-Influenza A/H7 (Eurasian Lineage) Assay Fact Sheet for Patients.

D. CDC will inform state and/or local public health authority(ies) of this EUA, including the terms and conditions herein.

E. CDC will ensure that public health and other qualified laboratories using the authorized CDC Human Influenza Virus Real-Time RT-PCR Diagnostic Panel-Influenza A/H7 (Eurasian Lineage) Assay have a process in place for reporting test results to healthcare providers and federal, state, and/or local public health authorities, as appropriate.

F. CDC will track adverse events and report to FDA as required under 21 CFR Part 803.

G. Through a process of inventory control, CDC will maintain records of device usage.

H. CDC will collect information on the performance of the assay, and report to FDA any suspected occurrence of false positive or false negative results of which CDC becomes aware.

I. CDC is authorized to make available additional information relating to the emergency use of the authorized CDC Human Influenza Virus Real-Time RT-PCR Diagnostic Panel-Influenza A/H7 (Eurasian Lineage) Assay that is consistent with, and does not exceed, the terms of this letter of authorization.

J. Only CDC may request changes to the authorized CDC Human Influenza Virus Real-Time RT-PCR Diagnostic Panel-Influenza A/H7 (Eurasian Lineage) Assay Fact Sheet for Healthcare Providers or the authorized CDC Human Influenza Virus Real-Time RT-PCR Diagnostic Panel-Influenza A/H7 (Eurasian Lineage) Assay Fact Sheet for Patients. Such requests will be made by contacting FDA concerning FDA review and approval.

Public Health and Other Qualified Laboratories

K. Public health and other qualified laboratories will include with reports of the results of the CDC Human Influenza Virus Real-Time RT-PCR Diagnostic Panel-Influenza A/H7 (Eurasian Lineage) Assay the authorized Fact Sheet for Healthcare Providers and the authorized Fact Sheet for Patients.

L. Public health and other qualified laboratories will perform the assay on an Applied Biosystems 7500 Fast Dx Real-Time PCR Instrument with the appropriate software.

M. Public health and other qualified laboratories will have a process in place for reporting test results to healthcare providers and federal, state, and/or local public health authorities, as appropriate.

N. Public health and other qualified laboratories will collect information on the performance of the assay, and report to CDC any suspected occurrence of false positive or false negative results of which public health and other qualified laboratories become aware.

CDC, Public Health and Other Qualified Laboratories

O. CDC, public health and other qualified laboratories will ensure that any records associated with this EUA are maintained until notified by FDA. Such records will be made available to FDA for inspection upon request.

The emergency use of the authorized CDC Human Influenza Virus Real-Time RT-PCR Diagnostic Panel-Influenza A/H7 (Eurasian Lineage) Assay as described in this letter of authorization must comply with the conditions above and all other terms of this authorization.

V. Duration of Authorization

This EUA will be effective until the declaration of emergency is terminated under section 564(b)(2) of the Act or the EUA is revoked under section 564(g) of the Act.

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Margaret A. Hamburg, M.D.
Commissioner of Food and Drugs